Shabeer. N,

Department of Biotechnology, Jamal Mohamed College, Tiruchirappalli - 620020

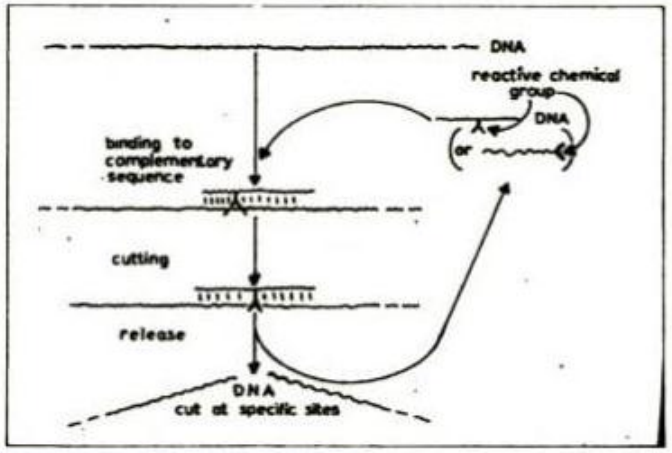
Genetic Engineering without Enzymes

THE TOOL KIT of the genetic engineer consists largely of a selection of enzymes that can be used to cut, alter, stitch and copy genetic material on demand. These enzymes are very specific —cutting, for example, only at particular sites of defined nucleotide sequence. A more generally useful set of tools would retain the specificity of enzymes, but would place it under our control; allowing scientists to manipulate *any* desired nucleotide sequence rather than being limited by the natural preferences of enzymes.

As a first step towards such a versatile specific toolkit, two separate teams of American scientists have found a way to cut single-stranded DNA anywhere they choose.

The general strategy is very simple (see Figure). First, a short stretch of DNA is made which can bind by base-pairing to the DNA sequence you wish to cut open. This "complementary DNA probe" is then linked to some reactive chemical group which, like a pair of molecular "scissors", is able to cut the backbone of DNA. The activated probe can then be added to the target DNA under conditions that allow it to bind to the target sequence and cut it open.

Using the same overall strategy (but different probes) Barbara Chu and Leslie Orgel of the Salk Institute, and Geoffrey Dreyer and Peter Dervan at Caltech, consistently cut target DNAs at or very close to particular chosen sites (*Proceedings of the US National Academy of Sciences*, vol 82, p 963 and p 968).



Cutting DNA without enzymes. A DNA probe is made and attached to a chemical group that can snip DNA. These "molecular scissors" are made specific by altering the sequence of nucleotides in the DNA probe

These reactions did not quite have the exquisite specificity of enzymes. Chu and Orgel found that the cutting took place anywhere within a stretch of DNA about 9 nucleotides long; while Dreyer and Dervans' scissors cut a swathe spread across a 16 nucleotide long region. But both groups are hopeful that this reasonable specificity will be further improved as the technique develops.

The technique seems equally suited to cutting RNA, and could develop into a very useful addition to the genetic engineer's tool kit. It may make it easier to investigate and exploit the genetic information of large genomes (the total collection of genes on a chromosome) by chopping them up into specific short sections. It may assist studies of gene control and gene activity by allowing particular messenger RNAs to be cut up and therefore destroyed. It may even find eventual use in chemotherapy as a means of destroying the DNA or RNA of pathogens such as viruses.

The possibilities will broaden considerably if the same basic strategy can be applied to things other than simply cutting target nucleic acids. By linking different reactive chemical groups to the DNA probes it may become possible to mutate and modify chosen sites on DNA or RNA in a whole series of different and highly specific ways. Provided they can be made sufficiently specific, these simple and versatile "enzyme-analogues" might have a big future. □